

**WHAT IS CLAIMED IS:**

- 1                   1.       A method for modulating the plasma circulation half-life of an active  
2 agent, said method comprising:
  - 3                   (a) providing a liposome having free active agent and precipitated active agent  
4 encapsulated therein; and
  - 5                   (b) varying the amount of said active agent that is precipitated in said  
6 liposome.
- 1                   2.       The method of claim 1, wherein step (b) comprises varying said active  
2 agent to lipid ratio.
- 1                   3.       The method of claim 2, wherein said active agent to lipid ratio is varied  
2 by the addition of an empty liposome.
- 1                   4.       The method of claim 1, wherein step (b) comprises varying the size of  
2 said liposome.
- 1                   5.       The method of claim 1, wherein step (b) comprises adding a  
2 component that enhances precipitation of said active agent.
- 1                   6.       The method of claim 5, wherein said component is a mono-, di-, tri-, or  
2 polyvalent anion.
- 1                   7.       The method of claim 1, wherein step (b) comprises varying both said  
2 active agent to lipid ratio and the size of the liposome.
- 1                   8.       The method of claim 1, wherein said active agent is an antineoplastic  
2 drug.
- 1                   9.       The method of claim 8, wherein said antineoplastic drug is a  
2 camptothecin.
- 1                   10.      The method of claim 9, wherein said camptothecin is a member  
2 selected from the group consisting of irinotecan, topotecan, 9-amino camptothecin, 10,11-  
3 methylenedioxy camptothecin, 9-nitro camptothecin, TAS 103, 7-(4-methyl-piperazino-  
4 methylene)-10, 11-ethylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-  
5 20(S)-camptothecin.

- 1                   **11.**    The method of claim **10**, wherein said camptothecin is topotecan.
- 1                   **12.**    The method of claim **1**, wherein said active antineoplastic drug is a  
2    vinca alkaloid.
- 1                   **13.**    The method of claim **12**, wherein said vinca alkaloid is a member  
2    selected from the group consisting of vincristine, vinblastine, vinorelbine and vindesine.
- 1                   **14.**    The method of claim **1**, wherein the precipitated active agent  
2    encapsulated in said liposome is at least 50% of said total active agent.
- 1                   **15.**    The method of claim **14**, wherein the precipitated active agent  
2    encapsulated in said liposome is at least 60% of said total active agent.
- 1                   **16.**    The method of claim **15**, wherein the precipitated active agent  
2    encapsulated in said liposome is at least 70% of said total active agent.
- 1                   **17.**    The method of claim **1**, wherein said liposome comprises  
2    sphingomyelin and cholesterol.
- 1                   **18.**    The method of claim **17**, wherein said liposome comprises  
2    sphingomyelin and cholesterol in a 55:45 ratio.
- 1                   **19.**    The method of claim **1**, wherein the plasma circulation half-life of said  
2    active agent is modulated for optimum efficacy.
- 1                   **20.**    The method of claim **1**, wherein the ratio of said active agent to lipid is  
2    about 0.005-1:1 (w/w).
- 1                   **21.**    The method of claim **20**, wherein the ratio of said active agent to lipid  
2    is about 0.05-0.9:1 (w/w).
- 1                   **22.**    The method of claim **21**, wherein the ratio of said active agent to lipid  
2    is about 0.1-0.5:1 (w/w).
- 1                   **23.**    A method for modulating the plasma circulation half-life of an active  
2    agent, said method comprising:

3 (a) providing a liposome having free active agent and precipitated active agent  
4 encapsulated therein; and

5 (b) adding a liposome with no encapsulated active agent.

1 **24.** The method of claim **23**, wherein the ratio of liposomes containing  
2 active agent to liposomes with no encapsulated agent is from about 1:0.5 to 1:1000.

1 **25.** The method of claim **24**, wherein the ratio of liposomes containing  
2 active agent to liposomes with no encapsulated agent is from about 1:1 to 1:100.

1 **26.** The method of claim **25**, wherein the ratio of liposomes containing  
2 active agent to liposomes with no encapsulated agent is from about 1:2 to 1:10.

1 **27.** The method of claim **26**, wherein the ratio of liposomes containing  
2 active agent to liposomes with no encapsulated agent is from about 1:3 to 1:5.

1 **28.** The method of claim **23**, wherein said active agent is an antineoplastic  
2 drug.

1 **29.** The method of claim **28**, wherein said antineoplastic drug is a  
2 camptothecin.

1 **30.** The method of claim **29**, wherein said camptothecin is a member  
2 selected from the group consisting of irinotecan, topotecan, 9-amino camptothecin, 10,11-  
3 methylenedioxy camptothecin, 9-nitro camptothecin, TAS 103, 7-(4-methyl-piperazino-  
4 methylene)-10, 11-ethylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-  
5 20(S)-camptothecin.

1 **31.** The method of claim **30**, wherein said camptothecin is topotecan.

1 **32.** A liposomal formulation, said liposomal formulation comprising:

2 a) an antineoplastic drug; and

3 b) a liposome having free antineoplastic drug and precipitated  
4 antineoplastic drug, wherein the precipitated antineoplastic drug in said liposome is at least  
5 50% of the total antineoplastic drug.

1 **33.** The liposomal formulation of claim **32**, wherein said antineoplastic  
2 drug is a camptothecin.

1                   **34.**     The liposomal formulation of claim **33**, wherein said camptothecin is a  
2 member selected from the group consisting of irinotecan, topotecan, 9-amino camptothecin,  
3 10,11-methylenedioxy camptothecin, 9-nitro camptothecin, TAS 103, 7-(4-methyl-  
4 piperazino-methylene)-10, 11-ethylenedioxy-20(S)-camptothecin and 7-(2-N-  
5 isopropylamino)ethyl)-20(S)-camptothecin.

1                   **35.**     The liposomal formulation of claim **34**, wherein said camptothecin is  
2 topotecan.

1                   **36.**     The liposomal formulation of claim **33**, wherein said antineoplastic  
2 drug is a vinca alkaloid.

1                   **37.**     The liposomal formulation of claim **32**, wherein the free antineoplastic  
2 drug and the precipitated antineoplastic drug are different.

1                   **38.**     The liposomal formulation of claim **36**, wherein said vinca alkaloid is a  
2 member selected from the group consisting of vincristine, vinblastine, vinorelbine and  
3 vindesine.

1                   **39.**     The liposomal formulation of claim **32**, wherein the ratio of said  
2 antineoplastic drug to lipid is about 0.005-1:1 (w/w).

1                   **40.**     The liposomal formulation of claim **39**, wherein the ratio of said  
2 antineoplastic drug: said lipid is about 0.05-0.9:1 (w/w).

1                   **41.**     The liposomal formulation of claim **40**, wherein the ratio of said  
2 antineoplastic drug: said lipid is about 0.1-0.5:1 (w/w).

1                   **42.**     The liposomal formulation of claim **32**, wherein said liposome  
2 comprises sphingomyelin and cholesterol.

1                   **43.**     The liposomal formulation of claim **42**, wherein said liposome  
2 comprises sphingomyelin and cholesterol in a 55:45 ratio.

1                   **44.**     The liposomal formulation of claim **32**, further comprising a liposome  
2 with no encapsulated active agent.

1                   **45.**     The liposomal formulation of claim **44**, wherein the ratio of liposomes  
2     containing active agent to liposomes with no encapsulated agent is from about 1:0.5 to  
3     1:1000.

1                   **46.**     The liposomal formulation of claim **45**, wherein the ratio of liposomes  
2     containing active agent to liposomes with no encapsulated agent is from about 1:1 to 1:100.

1                   **47.**     The liposomal formulation of claim **46**, wherein the ratio of liposomes  
2     containing active agent to liposomes with no encapsulated agent is from about 1:2 to 1:10.

1                   **48.**     The liposomal formulation of claim **47**, wherein the ratio of liposomes  
2     containing active agent to liposomes with no encapsulated agent is from about 1:3 to 1:5.

1                   **49.**     A liposomal formulation, said liposomal formulation comprising:  
2                   a)     an active agent;  
3                   b)     a liposome having free active agent and precipitated active agent  
4     encapsulated therein; and  
5                   c)     an empty liposome.

1                   **50.**     The liposomal formulation of claim **49**, wherein the ratio of liposomes  
2     containing said active agent to said empty liposomes is from about 1:0.5 to 1:1000.

1                   **51.**     The liposomal formulation of claim **50**, wherein the ratio of liposomes  
2     containing said active agent to said empty liposomes is from about 1:1 to 1:100.

1                   **52.**     The liposomal formulation of claim **51**, wherein the ratio of liposomes  
2     containing said active agent to said empty liposomes is from about 1:2 to 1:10.

1                   **53.**     The liposomal formulation of claim **52**, wherein the ratio of liposomes  
2     containing said active agent to said empty liposomes is from about 1:3 to 1:5.

1                   **54.**     The liposomal formulation of claim **49**, wherein said active agent is an  
2     antineoplastic drug.

1                   **55.**     The liposomal formulation of claim **54**, wherein said antineoplastic  
2     drug is a camptothecin.

1                   **56.**    The liposomal formulation of claim **55**, wherein said camptothecin is a  
2 member selected from the group consisting of irinotecan, topotecan, 9-amino camptothecin,  
3 10,11-methylenedioxy camptothecin, 9-nitro camptothecin, TAS 103, 7-(4-methyl-  
4 piperazino-methylene)-10, 11-ethylenedioxy-20(S)-camptothecin and 7-(2-N-  
5 isopropylamino)ethyl)-20(S)-camptothecin.

1                   **57.**    The liposomal formulation of claim **56**, wherein said camptothecin is  
2 topotecan.

1                   **58.**    The liposomal formulation of claim **57**, wherein said antineoplastic  
2 drug is a vinca alkaloid.

1                   **59.**    The liposomal formulation of claim **58**, wherein said vinca alkaloid is a  
2 member selected from the group consisting of vincristine, vinblastine, vinorelbine and  
3 vindesine.

1                   **60.**    The liposomal formulation of claim **49**, wherein the ratio of said active  
2 agent to lipid is about 0.005-1:1 (w/w).

1                   **61.**    The liposomal formulation of claim **60**, wherein the ratio of said active  
2 agent to lipid is about 0.05-0.9:1 (w/w).

1                   **62.**    The liposomal formulation of claim **61**, wherein the ratio of said active  
2 agent to lipid is about 0.1-0.5:1 (w/w).

1                   **63.**    The liposomal formulation of claim **49**, wherein said liposome  
2 comprises sphingomyelin and cholesterol.